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ORIGINAL MEMOIRS.

THE VALUE OF THE DIFFERENTIAL LEUCOCYTE COUNT IN ACUTE SURGICAL DISEASES.¹

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THE systematic examination of the various elements comprising the white cells of the blood, the so-called "differential count," has been extensively used in the last two years in the surgical clinics of this city. These researches have been particularly on the increase of the polynuclear cells in inflammatory conditions, especially in disease of the appendix and its sequelae.

Material for this paper has been furnished chiefly by blood examinations made in my service at St. Luke's Hospital during the year 1905. A very few examinations date back to 1904; and by the kind courtesy of my colleagues Dr. Robert Abbe and Dr. Farquhar Curtis, enough counts have been added to raise the number to about two hundred examinations.

The differential counts are made by the *personnel* of the Pathological Laboratory of St. Luke's Hospital, which is admirably conducted by Professor F. C. Wood; and there is every

¹ Read before the New York Surgical Society, January 24, 1906.

reason to believe that these examinations are made in the most approved manner, and that they are thoroughly reliable.

Although so much material must now be available, little or no attempt has as yet been made by the surgeon to draw practical deductions from such data.

The most satisfactory contribution to the subject is the paper of Dr. F. E. Sondern, "The Present Status of Blood Examinations in Surgical Diagnosis,"² which puts the subject on a thoroughly practical basis.

The reason so little authoritative comment on the value of this method has been made is doubtless a more or less general impression that the findings are merely an elaboration of the leucocyte count rather than, as I hope to demonstrate, a quite different and much more important element.

When the differential count first began to attract interest, the value of the ordinary leucocyte count had become much discredited by many, perhaps most, surgeons. This distrust was certainly felt by the writer, who had ceased to pay more than a minimum of attention to such findings.

Even as recently as September, 1905, one gets from the report of the First International Congress of Surgery, at which examination of the blood was made a major subject, nothing of the importance of the new investigation, it being mentioned only casually, and with no attempt to emphasize its special features.

Just as the original leucocyte count had its pitfalls, the differential count, it must be admitted, has its individual drawbacks. It needs, even more than the older method, a considerable knowledge of the subject and ability to interpret judiciously the several pathological variations. This knowledge, however, can be applied much more surely, with fewer mistakes and far greater positive and helpful results.

The value of this method depends not on the significance of any given quantities, X or Y representing the number of the leucocytes or of the polymorphs. It does not depend at all

² Medical Record, March 25, 1905.

on the absolute percentage of the polymuclear cells, a method almost as valueless as the leucocyte count alone, but on the *relative proportion* of the polymuclear cells to the total leucocytosis.

To understand this relation, it is necessary to consider very briefly some elementary facts and also the standard which the writer has adopted in studying the results of the differential count.

Normal Leucocytosis.—Variable quantity, influenced by age, variations in habit, time of day, food, exercise, etc. Average varies, according to different authors. Somern gives the average as 6700. The writer has thought it wise to consider 10,000 as the extreme limit of ordinary normal leucocytosis, believing that this estimate will correct errors of idiosyncrasy, etc.

Hyperleucocytosis, then, would mean counts in excess of 10,000.

Hypoleucocytosis is still harder to determine and without special reasons should not be so considered except distinctly under 5000, with a considerable reserve for personal idiosyncrasies. The surgeon is generally more interested,—certainly in acute inflammations,—in an *increase* rather than a decrease of leucocytosis.

Leucocytosis in inflammation is an index of reaction rather than of the absolute severity of the particular kind of infection.

As we shall see later, there are a number of fatal cases with a distinct lowering of the leucocytosis.

Somern says: "Leucocytosis is largely dependent on body resistance towards infection, and therefore the degree of increase can be no guide to the intensity of the pathological process. Good resistance will produce pronounced leucocytosis even in slight infections, and poor resistance but little leucocytosis in slight infections and possibly none at all in grave infections. No adequate clinical method exists by which this body resistance can be determined with sufficient accuracy to apply it as a factor to the leucocyte count; and this is the key

to the disappointment encountered by the surgeon in utilizing these counts in diagnosis."

What is the normal proportion of polynuclear cells? The normal ratio is again estimated differently by various authors. Sondern's average is 68 per cent. Most authorities put it somewhat higher. Von Lembeck, quoted by Cabot, puts it at 70 to 80.

The writer has thought it wise, as in the case of the leucocyte count, to adopt the rather higher average corresponding perhaps more accurately to what is called hyperleucocytosis, and has adopted 75 per cent. as a working average.

In infancy there is a very marked diminution of the proportion of polynuclear cells, said to be from 28 to 40 per cent. The writer's cases show in infants with pathological conditions a strikingly low polynuclear count,—e.g., child of six weeks, fatal intestinal obstruction, total leucocytosis 16,200 per cent., polynuclear cells, 14. Child 1 year, acute otitis media, total leucocytosis 13,300 per cent.; polynuclear cells, 31.

The Behavior of the Polynuclear Cells; Cells in Acute Inflammatory Conditions.—Generally speaking, there is a rise in the percentage of the polynuclears which is a fair index of the severity of the process, but it must be strongly emphasized that it is *per se* far from being an absolute guide; for if we should rely *alone* on the increase of the polynuclear cells, we should have but little more information than was furnished by the older method. For it must be remembered that we may have,—even though it be rare,—a very high percentage of polynuclear cells without a very serious or fatal result. Sondern says in his experience more than 94.5 was always fatal.

Personal experience furnishes a notable exception. Man, age 74, advanced tuberculosis of the testicle; per cent. polynuclear, 97.5. A case of gangrenous appendix, very ill, was saved by operation; polynuclear 94.5. A case of "catarrhal appendicitis," recovering without operation; leucocytosis, 20,600; polynuclear, per cent., 94.

As a matter of fact, a very high percentage of polynuclear

cells (infants not computed) is not the rule in fatal cases as the average in these recorded cases was: Total leucocytosis of 13,000, per cent. polymuclears, 82.9; showing a disproportion of five counts in the "standard" chart.

Some instances of low polymuclear per cent. in fatal cases: Gangrene of the lung, 57 per cent.; pyemia, 67; general peritonitis, 69.

Dr. Sondern's findings are: "In adults a purulent exudate or a gangrenous process is decidedly uncommon with less than 80 per cent. of polymuclear cells, and the probability of their presence increases with their percentage."

While admittedly true, this statement has too many exceptions not to call for some special comment, as may be noted from the following cases: General peritonitis, 69 per cent.; general peritonitis, 75 (two cases) appendicular abscess, 77; pyosalpinx, 76; pyosalpinx, 75½; gangrene of skin, 59; gangrene of leg, 75; abscess of lung, 57; acute pelvic abscess, 66.5; ischio-rectal abscess, 77; pyemia, 67; perinephritic abscess, 72; acute suppurative nephritis, (three counts,) 68, 55, 62.

So that we must look further for some value inherent to the polymuclear count than the mere degree which it may attain. Its real value in the writer's judgment is to be found in another and distinct feature, viz., *the relative disproportion of the polymuclear percentage to the total leucocytosis*. This is the feature which Dr. Sondern has so clearly pointed out, and constitutes the chief topic of the present contribution.

In this matter, the question of body resistance, necessarily conjectural, must be taken into account; but it is probably more clearly defined by this disproportion than by any means at present in our command.

The writer's experience and observation lead him to believe that with a moderate use of the total leucocytosis there should be in favorable cases a moderate rise only of the polymuclear cells, showing that the infection is localized and absorption is limited.

On the other hand, if there is only a moderate leucocytosis

with a *notable increase* in the polymuclear cells, it indicates almost unquestionably that there is either a severer form of lesion or that there is less resistance to absorption, or that both of these conditions exist.

As examples of good resistance (see chart) the following examples may be quoted:

	Leucocytosis.	Polymuclear, percent.
1. Appendicular abscess,.....	14,000	77
2. Appendicular abscess,.....	18,000	78½
3. Acute appendix,.....	20,000	78

While as examples of a severe lesion (note steep line of this second group rising from the leucocyte side of the chart to the polymuclear side):

4. Acute gangrenous appendix,.....	4400	81	Died
5. Acute appendix and general peritonitis,	10,600	83	"
6. Intestinal obstruction,.....	7400	81.5	"
7. Septic endometritis, general peritonitis,	17,800	97.5	"
8. Gangrenous appendix,.....	9500	94.5	Cured
9. Appendicitis, general peritonitis,....	13,200	86	Died
10. Septic endometritis, general peritonitis,	14,000	91.5	"

This *disproportionate* increase of the polymuclears is on the whole more reliable than any of the other data, and has served greatly to influence the writer's work in the past year. The exceptions have been few; in no case has he actually been led astray, though occasionally the lesion has been of lesser severity than anticipated. There is, however, a good deal to be said on this last point, particularly on the important subject of appendicitis. We operate now usually so promptly that we find the lesions relatively less advanced than formerly, while some of these seemingly mild processes may potentially have the worst possibilities. My colleague, Dr. Curtis, for instance, informs me that he removed a rather mild-looking appendix that was productive of very acute symptoms and a high differential count, but inoculations from the contents of the appendix yielded a virulent culture of streptococci.

TOTAL LEUCOCYTES

PER CENT. POLYNUCLEARS

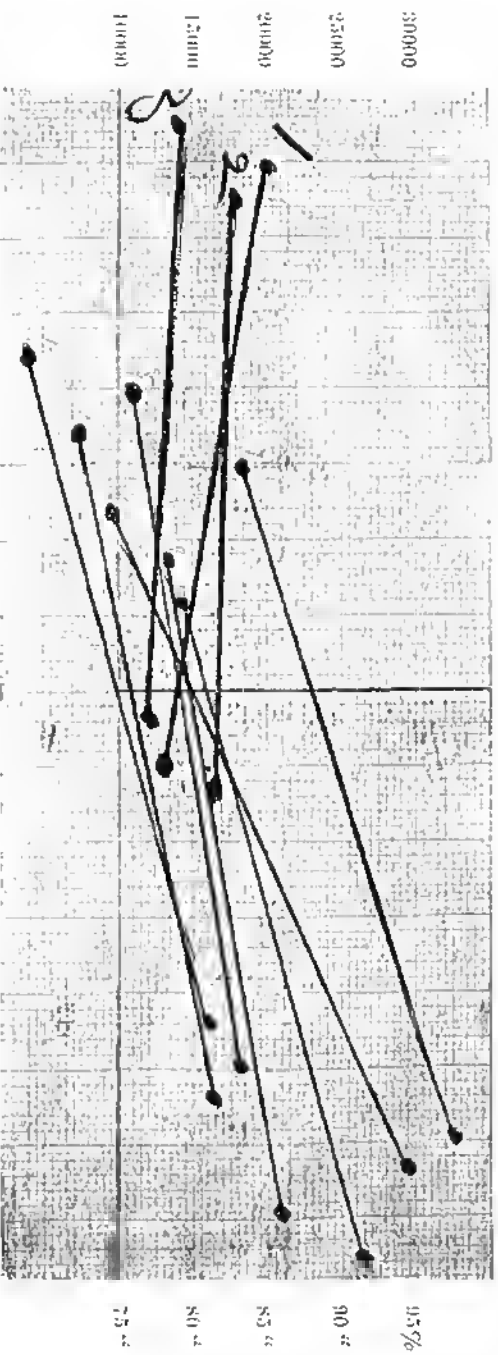


CHART 1.

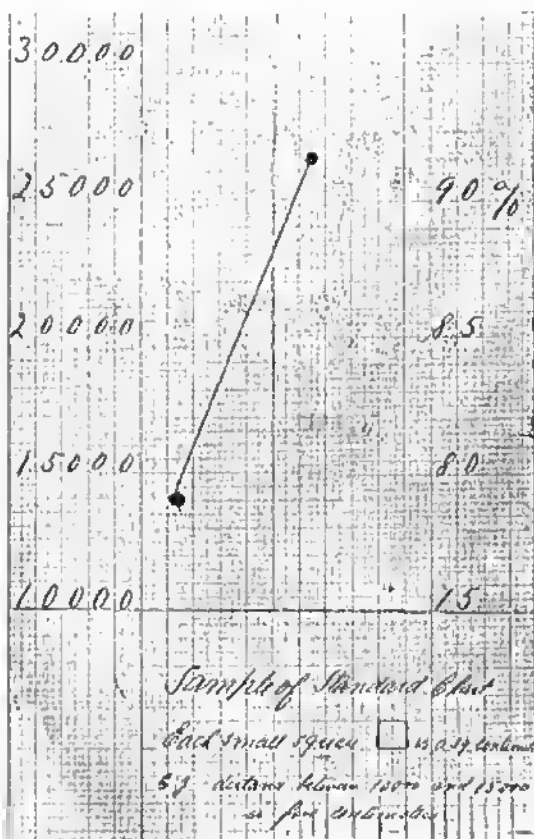


CHART 2.

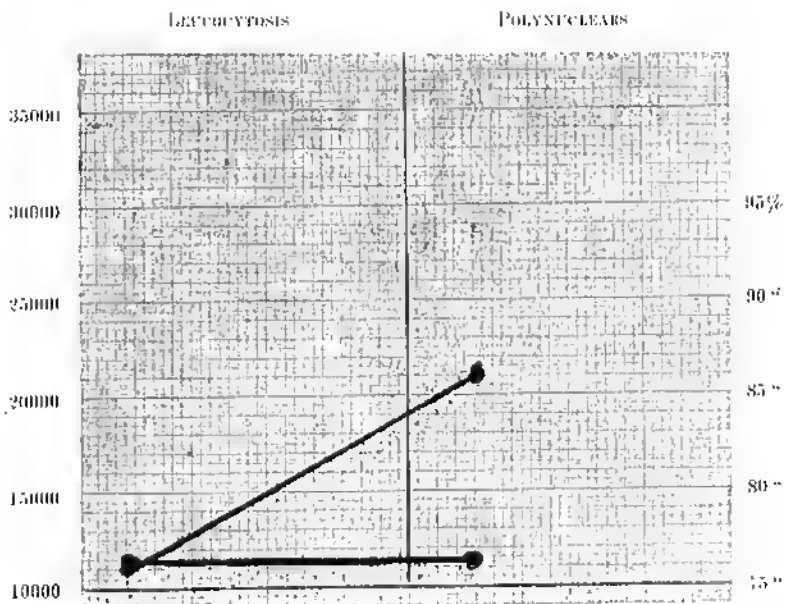


CHART 3.

What shall be the standard by which we shall gauge various degrees of disproportion between the leucocyte count and the percentage of polymuclear cells? As we have no definite means of measuring body resistance, it is necessary in the present state of our knowledge to resort to avowedly arbitrary standards.

It has seemed to the writer that in inflammations which are well resisted, the polymuclear cells are increased approximately one degree for every one thousand of the total leucocytosis above ten thousand. Starting with such a basis, experimental charts have been worked out and the results seem on the whole to show that such a standard forms a very good working basis for the measurements which have been adopted by the writer. (Chart II.)

Description of the Standard Chart.—The chart is divided into units of one centimetre allowing an easy and practical computation of the results. A horizontal base-line is drawn as the starting point of the pathological leucocytosis of ten thousand on the left-hand side, while the other or right-hand end of the base-line corresponds with the index of 75 per cent. polymuclear cells, the limit more or less arbitrarily chosen. Variations in these proportions are indicated by making a dot at the proper level of the left-hand or leucocytosis side of the chart, while a similar dot at the proper level of its percentage is made on the polymuclear side of the chart. For purposes of convenience these two dots are connected by a straight line. The vertical distance between the two dots will represent in the accepted counts (one centimetre) the disproportion between the two counts. (Chart III.)

E. g.—suppose on the left a dot indicating a leucocyte count of 11,000 and on the right a dot indicating 76 per cent. polymuclear cells, the result would be indicated by a line which would be absolutely horizontal, and would be indicative of a just proportion between the two elements of the count.

If, however, with the same leucocytosis of 11,000 there were a polymuclear increase to 86 per cent. the line connecting

these two points would have a steep rise from left to right and measurement of the vertical distance between these two points would give ten centimetres or ten units.

Thus we have something definite to compute, and we could speak of a five unit or a ten unit or a fifteen unit disproportionate increase or decrease of the polymuclear cells.

Such a chart moreover is particularly useful in continued examinations from day to day, as the fluctuations can be readily read and expressed in definite counts, such accurate comparisons being lacking heretofore.

If a large number of observers would collect extensive data by using such a standard chart, utilizing these units to record their findings we might hope eventually to strike working averages and standards on which to base future observations.

The writer feels that it would be presumptuous and unsafe to attempt as yet to lay down any rules from his limited findings with such a chart.

He hopes, however, that others may be encouraged to adopt the standard which is hereby tentatively offered, and, it is hoped, improve on it.

Speaking very generally and with considerable reserve, the writer attaches already considerable significance to the findings which some of these charts have shown.

If the line connecting the levels of the leucocyte count and the polymuclear count runs pretty nearly horizontal, whether up or down, only 2 to 4 units difference, it indicates a lesion that whether severe or not, is well borne and therefore of a good prognosis.

Lines running *upward* from the leucocyte side towards the polymuclear indicate in general a rather severer lesion and less resistance. If the interval between the two points is considerable, say ten or more units, we are quite sure to have a pretty severe lesion. The majority (about $\frac{2}{3}$) of total cases of all kinds show a rising line, and as we shall see later in such a condition as appendicitis, fatal cases have *all* a rising line. (Chart IV.)

LEUCOCYTOSIS

POLYNUCLEARS

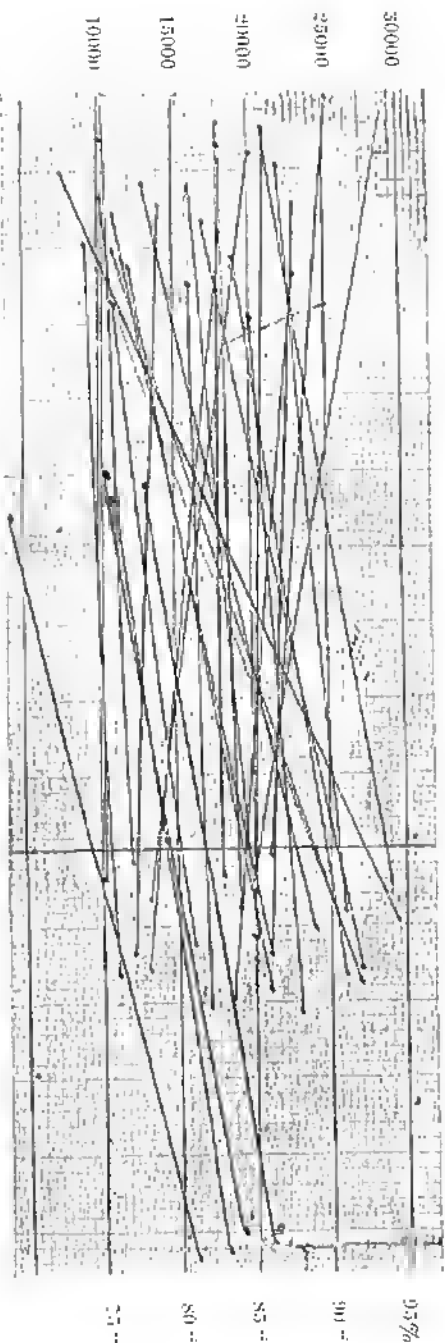


Chart 4.—Acute Appendicitis.

THE DIFFERENTIAL COUNT IN SPECIAL CONDITIONS.

Appendicitis.—In twenty acute cases a *distinct* disproportionate increase of the polymuclears indicated by a *rising* line was manifest.

In two cases the line was very nearly horizontal, showing a good balance between the two elements.

In three cases there was a distinct downward tendency of the line, showing preponderance of leucocytes.

These results seem to show a positive value for the differential blood-count as estimated by the standard chart.

There was one exception: Mild case of catarrhal appendicitis, allowed to convalesce without operation. A single examination showed leucocytosis 24,600; polymuclear, 94 per cent.; giving a rise of four units.

All the severer lesions, those with gangrene of the appendix or progressive peritonitis, and *all* the fatal cases, showed a *rising* line on the standard chart, while all the cases indicated by a falling line were distinctly mild types such as well-defined "safe" abscesses with little febrile or constitutional disturbances. As it is in the severer cases, particularly those in which the initial symptoms are obscure or perplexing, that we can least afford to make mistakes, the great value of the polymuclear increase is evident, as the findings on these cases will hardly ever lead us astray.

A case of this nature first definitely called my attention to the value of the method in question:

Man 28, who for twenty-four hours had had a chain of acute abdominal symptoms, obstinate vomiting, general abdominal pain, moderate rise of temperature and pulse; looked sick. Examination of the abdomen quite negative as regards ordinary signs of appendicitis. A little tenderness just above the pubes was noted, but it was said to be habitual. Rectal examination elicited some tenderness on pressure against the posterior wall.

Differential count by Dr. Soule: Leucocytosis, 22,800;

polymuclears 88 per cent. When seen six hours later, general remission of all symptoms, felt and looked better.

Strengthened by Dr. Sondern's personally expressed opinion, I had made a diagnosis of gangrenous appendix which was probably permanently fixed in the pelvis. The patient was immediately taken to St. Luke's Hospital, but two of the best consultants failing to confirm my views; operation was deferred for twenty-four hours, by which time the condition was obvious. Operation showed great meteorism, general reddenening of the intestine, a little turbid serum and finally a gangrenous appendix in the pelvis. Death from progressive peritonitis.

The above experience, so far as the correctness of the findings is concerned, has been frequently repeated, and did space allow many similarly impressive instances could be cited.

The importance of a disproportionate increase of the polymuclears (rising line on the chart) particularly if progressive, cannot be overrated, and those wilfully disregarding such evidence are perhaps not exhausting all resources of diagnosis.

If one examination in a threatening case of appendix shows for example 15,000 leucocytes and 85 per cent. polymuclears, a difference of five units by the "standard" chart, and a second later examination shows the same leucocytosis with a rise of the polymuclears to 87 per cent., the condition must be regarded as considerably worse, both as regards the increasing severity of the lesion and the diminishing ability to withstand it.

Chronic Appendicitis.—These cases of interval operation showed on the whole little leucocytosis and practically no disproportion on the chart, viz.: Five cases showed a falling line on the chart; five cases showed a stationary line or an insignificant rise.

Female Genitalia.—The differential in pyosalpinx:

	Leucocytosis.	Polymuclear, percent.
1.	22,300	87
2.	12,000	76
3.	8700	75.5

	Leucocytosis.	Polynuclear, percent.
4.	11,000	82.5
5.	15,000	76.5
6.	8000	66.5
7.	13,600	81.5
8.	16,400	88
Average percent, polynuclear,.....		77.5
Septic endometritis,.....	17,800	97.5 Died
Septic endometritis,.....	12,000	75 Cured
Septic endometritis, general peritonitis.	21,800	91.5 Died

The differential count in pyosalpinx was absolutely consistent. The chronic cases with little temperature showed an average of 70-75 per cent., the acute cases a little over 80 per cent. None reached any of the extreme ranges which would have been inconsistent with such a well-limited inflammation, while in the case of septic endometritis peritonitis there was attained the maximum polynuclear count 97½ per cent., which with a leucocytosis of 17,800, gives a disproportionate increase of polynuclears of 16½ units, which speaks eloquently for the prognostic significance of these examinations and the method of computing these results.

Intestinal Obstruction and Cases of General Peritonitis.—Eight cases; one recovery. Average disproportionate use of polynuclears was $7\frac{3}{10}$ per cent. a high count whose value is self-evident.

Tuberculosis.—It is stated by some that there is a decrease, absolute and relative, of the polynuclear cells in tuberculosis. The writer's findings do not generally substantiate such views, the percentage of the polynuclears being generally a rising one.

	Leucocytosis.	Polynuclear, percent.
Tuberculosis of the peritoneum.....	8,800	86
Tuberculosis of the peritoneum.....	1,900	82
Tuberculosis of the spine.....	22,000	81
Tuberculosis of the hip.....	3,200	68
Tuberculosis of the kidney.....	23,200	72.5
Tuberculosis of the kidney.....	21,000	84
Tuberculosis of the testicle.....	23,000	97½

This last polymuclear increase of $97\frac{1}{2}$ is the largest occurring in the series, it being also observed in a case of fatal septic endometritis. Only once has the author noted a higher percentage, a case of suppurative meningitis, $99\frac{1}{2}$, quoted by Cabot.

Biliary Tract.—Observations as regards reaction to gall-stones without infection showed only negative data, while in two fatal cases of empyema of the gall-bladder there were rises on the standard chart of four units in one case and five and a-half in another case, those findings being particularly significant. The patient was extremely ill. The huge suppurating gall-bladder was easily and quickly shelled out of its bed without contamination of the wound, which was liberally packed and left open. The septic manifestations, however, continued to increase, although an autopsy disclosed an irreproachable condition of the site of the operative manipulation. In this case the increased proportion of the polymuclears $91\frac{1}{2}$, with a total leucocytosis of 21,000, must be interpreted as a significant warning of the intensity of the necessarily fatal septic absorption.

There is in most cases a postoperative or, more properly speaking, postanesthetic temporary leucocytosis. While the data at hand are insufficient to warrant any generalization, an impression was gained that the polymuclears behaved quite consistently in such cases, rising more or less proportionately with the leucocytosis and subsiding likewise.

In the convalescence after operation the relative differential count always proved itself of value, more particularly after abdominal section with wound infection, the differential count showing a rise of the polymuclears consistent with the temporary leucocytosis rather than a disproportionate increase which would have been suggestive of a progressive peritonitis.

It was of value in several cases of miscarriage or abortion in confirming the belief that we were dealing with the effects of the retention of the products of gestation rather than with septic infection.

It was of value several times, by the presence of a very low polymuclear (28 in one instance) in calling our attention or confirming our suspicions as to the probability of a typhoid fever.

As regards the value of a rise in the proportion of polymuclears as indicating the existence of a typhoid perforation, the writer has no direct data. Its value has been insisted on by some, and the disproportionate rise should naturally be expected with a progressive peritonitis, which surgically does not interest as much as our intervention must anticipate the peritonitis in order to expect success.

It is probable that there may be an antemortem rise in polymuclear cells in certain conditions which should not ordinarily produce such an increase.

A moribund cancer of stomach showed leucocytosis of 7800, polymuclears of 86, a difference of 13 units on the standard chart. Moribund double hydronephrosis from sarcoma of bladder temperature 100, leucocytosis 9900, polymuclears 90, a disproportionate rise of 15 units on the standard chart.

In the case of a stricture of the urethra with a chill and a rise of temperature to 105.6, quickly subsiding without sequelæ, there was an interesting prognostic negative count of polymuclears, only 63 per cent. to 16,000 leucocytosis.

Two prostates showed interesting counts. One was very large and tender and highly suggestive of the development of an abscess. There was only 63 per cent. polymuclears, with 10,000 leucocytosis; 24 hours later there was a marked remission of all symptoms, and entire cure followed.

In the other, a large abscess was evacuated; leucocytosis, 10,000; 24 hours later there was a marked remission of all symptoms, and entire cure followed.

There were several curious observations from the usual behavior of the polymuclears to be noted, and it is probable that there was in these cases some counteracting influence for which there is at present no proper explanation:

E. G., woman, 28, with foci of multiple miliary abscesses of the kidney, cured by resection of the upper and lower lobes of the left kidney. She ran an irregular and high pyemic temperature and yet there was not in four examinations a polymuclear percentage higher than 68, the leucocytosis ranging from 7400 to 9300. On the other hand, this patient may be explained as of prognostic value and denoting that the process was not of a severe nature. Another case, of a man extremely ill with acute pyemic symptoms, which seemed to point to suppuration of the liver, showed great variations in the proportions of the polymuclears, which at no time rose above $88\frac{1}{2}$, although he immediately succumbed to an exploration of the liver, which was not the site of an abscess, but showed a condition of general breaking down of the tissue.

A large number of corroborative examinations were made on persons with non-inflammatory and favorable surgical lesions, such as reducible hernia, prolapse of uterus, deformities, etc., to see if any data might be developed which would invalidate our surmises as to what constitutes normal or abnormal differential counts; but in no instance was any inconsistency noted.

This investigation has covered only the behavior of the polymuclear cells as it was thought inadvisable to consider other elements from lack of sufficient material.

Attention should be called to one property of the eosinophiles, which seems not to appear in many of the recent works on blood, namely: the increase in gonorrhœa, which was found not infrequently in these observations, in one case as high as 6 per cent. in a case of gonorrhœal rheumatism, with a latent urethral lesion.

CONCLUSIONS.

The differential blood-count and its relation to the total leucocytosis is today the most valuable diagnostic and prognostic aid in acute surgical diseases that is furnished by any of the methods of blood examination.

It is of value chiefly in indicating fairly consistently the existence of suppuration or gangrene, as evidenced by an increase of the polymuclear cells disproportionately high as compared to the total leucocytosis.

The greater the disproportion the surer are the findings, and in extreme disproportions the method has proved itself practically infallible.

As the relative disproportion between the leucocytosis and the percentage of polymuclear cells is of so much more value than the findings based on a leucocyte count alone, this latter method should be abandoned in favor of the newer and more reliable procedure.

The negative findings showing no relative increase or even an actual decrease of the proportion of the polymuclear cells while of less value, shows with rare exceptions the absence of the severer forms of inflammation.

In its practical applications, the method is of more frequent value in the interpretation of the severity of the lesions of appendicitis and their sequelæ.

In order to have some standard to measure disproportion of the polymuclear percentage, it is suggested that a trial be made of the chart which is tentatively recommended under the arbitrary designation of "standard."